Contact Dermatitis: an Allergic Disease

Luz Fonacier MD, FACAAI, FAAAI
Head of Allergy & Immunology
Training Program Director
Winthrop University Hospital
Professor of Clinical Medicine
SUNY at Stony Brook

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Objectives:

1. Differentiate different causes of eczema and clues to the diagnosis of contact dermatitis
2. Discuss the relevant allergens in allergic contact dermatitis
3. Demonstrate the proper technique of patch testing and its interpretation

Inflammatory Skin Disorders

- **Dermatitis and Eczema**
  - Atopic D, Contact D, Seborrheic D, Pruritus, Nummular Eczema, Erythroderma, Lichen Simplex Chronicus/Prurigo Nodularis, Dyshidrosis, Pityriasis Alba
- **Papulosquamous disorders**
  - **Psoriasis**
  - **Parapsoriasis**
    - **Acute: Pityriasis lichenoides et varioliformis acuta**
    - **Chronic: Pityriasis Lichenoides Chronica**
    - **Lymphomatoid Papulosis**
  - ***Pityriasis***
    - ***Pityriasis Rosea***
    - **Pityriasis Rubra Pilaris**
  - ***Lichenoid***
    - **Lichen Planus**
    - **Lichen Nitidus**
- **Urticaria**
- **Erythema Multiforme/Drug Eruption:** SJS, TEN, E Nodosum
- **Other Erythemas:** E. Annulare, E Centrifugum, E Marginatum, E Toxicum, Necrolytic Migratory Erythema

Dermatitis of the Eyelid: Guidelines for Diagnosis

Main Risk Factor for the Diagnosis:

- Allergic Contact Dermatitis: 4-eyelid involvement
  (OR = 3.0; 95% CI, 1.1–8.1)
- Irritant Contact Dermatitis: Onset of symptoms within 2- 6 months from time of exam
  (OR = 2.1; 95% CI, 1.1–4.0)
- Atopic Dermatitis: Onset of symptoms >6 months (OR = 4.9) & personal history of atopy (OR=3.6)

Ayala F et al. Eyelid Dermatitis: An Evaluation of 447 Patients. Dermatitis 2003;14:069-074
* Sher M. Contact dermatitis of the eyelids. S Afr Med J 1979;55:511–513. (PubMed)

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Dermatitis of the Eyelid

- Allergic contact dermatitis: 55-63.5%
  (as high as 72% if eyelid alone *)
  - 13.4% Fragrances
    - 7.1% Fragrance Mix
    - 6.3% Balsam of Peru
  - 8.2% Gold sodium thiosulfate
    (most common allergen in pure eyelid dermatitis)
  - 6.0% Nickel sulfate
- Irritant contact dermatitis: 15%
- Atopic dermatitis: < 10%
- Seborrheic dermatitis: 4%

Ayala F et al. Eyelid Dermatitis: An Evaluation of 447 Patients. Dermatitis 2003;14:069-074

Reitschel RL et al. Common contact allergens associated with Eyelid dermatitis: data from the NACDG 2003-2004 study period. Dermatitis 2007; 18:78-81

*Valsecchi et al. Eyelid Dermatitis: an evaluation of 150 patients. Contact Dermatitis.1992;27:143-7

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Nickel: Contact Allergen of 2008

- 10% of population are nickel allergic
- Increasing incidence of allergic sensitization to nickel in North America
  - New sources of nickel ACD: cell phones
- New insight was offered into the possible genetics of nickel contact allergy

Irritant Contact Dermatitis

- Primary diagnostic criteria
  - Macular erythema, hyperkeratosis, or fissuring predominating over vesiculation
  - Glazed, parched, or scalded appearance of the epidermis
  - Healing begin promptly on withdrawal offending agent
  - Patch testing negative

- Minor objective criteria
  - Sharp circumscription of the dermatitis
  - Evidence of gravitational influence (dripping effect)
  - Less tendency for dermatitis to spread (than in ACD)
  - Morphologic changes suggest small differences in concentration or contact time producing large differences in skin damage

Rietschel RL, Fowler JF Jr. *Fisher's Contact Dermatitis*. 4th ed. Baltimore, Md: Lippincott Williams & Wilkins; 1995

Irritant Contact Dermatitis

Localized dermatitis without vesicles
Webs of fingers extending onto the dorsal & ventral surfaces ("apron" pattern), dorsum of hands, palms & ball of thumb

Allergic Contact Dermatitis

Often have vesicles
Favor the fingertips, nail folds, dorsum of the hands
Less commonly involve the palms

Sun CC, Guo YL, Lin RS. Occupational hand dermatitis in a tertiary referral dermatology clinic in Taipei. Contact Dermatitis 1995;33:414–418.
Picture adapted from: Erin Warshaw, Gina Lee, Francis J. Storrs. Hand Dermatitis: A Review of Clinical Features, Therapeutic Options, and Long-Term Outcomes. Dermatitis 2003;14:119-128

Hand Eczema
Most Common Irritant Contact Dermatitis

Regional Location of Hand Eczema

- Irritant CD: most common in palmar region
- Allergic CD: more common in dorsal hand & fingers
- Atopic Dermatitis: morphologically distinct involvement of dorsal hand surfaces combined with volar wrist

Simpson EL, Thompson MM, Hannifin JM. Prevalence and morphology of hand eczema in patients with Atopic Dermatitis. Dermatitis 2006:17:123-7

Pyoderma Gangrenosum

Main Variants

- Classic pyoderma gangrenosum
  - deep ulceration with violaceous border that overhangs the ulcer bed
  - most common on the legs
- Atypical pyoderma gangrenosum
  - Vesiculopustular, "juicy" usually only at the border; erosive or superficially ulcerated
  - often on dorsal surface of the hands, extensor of the forearms, or face
-

Pyoderma Gangrenosum

- 50% have systemic illnesses that may occur prior to, concurrently or following the diagnosis
- Arthralgias & malaise often present
- Commonly associated diseases
  - inflammatory bowel disease (ulcerative colitis or Crohn's disease)
  - seronegative or seropositive polyarthritis
  - hematologic disorders (leukemia, preleukemia, monoclonal gammopathies (primarily immunoglobulin A)
  - less common: psoriatic arthritis, osteoarthritis, spondyloarthropathy; hepatitis; SLE

Nummular eczema

- Pruritic
- Plaques of closely set, thin walled vesicles on erythematous base
- Clearly demarcated edge
- Limbs more than trunk
- Variable intermittent course
- ? High incidence of atopy

Contact Dermatitis from Cigarettes

- Occupational ACD in tobacco factory workers
  - Usually on workers' hands or widespread dermatitis
  - May be due to chemicals in cultivation & processing: waxes, paraffins, fatty acids, organic acids, aldehydes, ketones, phenols, paraphenols, ncatechols, & tannins
- Non-occupational ACD
  - dermatitis on 2nd & 3rd digits of hand
  - erythema, edema, scaling on lips
  - macules +/- pigmentation on upper lip

Zoey R. et al. Allergic Contact Dermatitis from Cigarettes. Dermatitis. 2009;20:6–13
Rycroft RJG. Tobacco dermatitis. Br J Dermatol 1980;103:225–8.

Cigarettes

- **Underreported & under recognized cause of ACD**
  - **~46 million smokers in the US**
  - **Nearly 3000 teens/day take up the habit of smoking**
- **Allergens from filters, paper, tobacco**
  - **Cocoa Products***
  - **Menthol: Mint & peppermint**
  - **Licorice***
  - **Colophony: released from cigarette paper & filters**
    - **associated with airborne ACD (occupational & non-occupational)**
    - **can cause asthma**
  - **Formaldehyde**

- **Patch Testing is recommended in smokers with dermatitis involving hands, face, & neck****

*main flavor additives in Philip Morris cigarettes

Zoey R. et al. Allergic Contact Dermatitis from Cigarettes. Dermatitis. 2009;20:6–13
Jones K, Garfitt SJ, Calverley A, Channa K. Identification of a possible biomarker for colophony exposure. Occup Med 2001;51: 507–9.
Watsky KL. Airborne allergic contact dermatitis from pine dust. Am J Contact Dermat 1997;8:118–20. Kato A, Shoji A, Aoki N. Contact sensitivity to cigarettes. Contact Dermatitis 2005;53:52–3
Sasaya N, Oiso N, Shigeru K, Kawada A. Airborne contact dermatitis from cigarettes. Contact Dermatitis 2007;56:173–4
*Dawn G, Fleming CJ, Forsyth A. Contact sensitivity to cigarettes and matches. Contact Dermatitis 1999;40:236–8

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Hypereosinophilic Syndrome

- Skin: Angioedema/urticaria, erythematous, pruritic papules & nodules
- Cardiac disease: major morbidity & mortality
- Neurologic complications: thromboembolic episodes, encephalopathy, peripheral neuropathy
- Respiratory: cough, Eos lung infiltrates
- GI: Eos gastritis, enterocolitis, colitis

Cutaneous T-Cell Lymphoma or Mycosis Fungoides

Stages:

- Patch (atrophic or nonatrophic)
  - Often goes on for many years
  - Patches with thin, wrinkled quality, often with reticulated pigmentation
  - Pruritus varies from minimal or absent to common in premycotic phase & may precede MF by years
  - Often on lower trunk & buttocks
- Plaque
- Tumor

Brachioradial Pruritus

- Sunlight induced chronic episodic pruritus localized to the outer aspect of elbow & adjacent lower & upper arms
- Commoner in fair-skinned people in tropical climates
- **Causes:** - probably "solar pruritus"
  - nerve damage from irritation of cutaneous branch of radial nerve or the cervical spine
- **Treatment:**
  Sun protection, camphor, menthol, cervical spine manipulation, capsaicin, topical anesthetic

Walcyk PJ *Br J Dermatol* 1986;115:177-80
Bech-Thomjsen N *Acta Dern Venereol (Stockh)* 1995;75:488-9

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Dermatophytide

- Secondary distant aseptic lesion
- Criteria
  - Proven focus of dermatophyte infection
  - Positive skin test to group-specific trichophytin antigen
  - Absence of fungi in the id lesion
  - Clearing of id after fungus is eradicated
- Patterns
  - Eczematous vesicles of hands & feet
  - Pityriasis-Rosea like
  - Erysipelas-like
  - Erythroderma

Papulosquamous Disorder

Papules +/- Plaques and scales
(scaly papules and plaques)

- **Psoriasis** (red, scaly lesions)
- **Parapsoriasis** (resembles psoriasis)
  - Large Plaque Parapsoriasis
  - Small Plaque Parapsoriasis
  - Pityriasis Lichenoides
    - Pityriasis lichenoides et varioliformis acuta
    - Pityriasis lichenoides chronica
  - Lymphomatoid papulosis
- ***Pityriasis*** (flaking or scaling)
  - *Pityriasis* Rosea
  - *Pityriasis* rubra pilaris
- ***Lichenoid*** *(resembles lichen: organisms consisting of a symbiotic association of a fungus*
  - Lichen Planus
  - Lichen Nitidus

Psoriasis

- Plaques typically have dry, thin, silvery-white or micaceous scale
- Removing the scale reveals a smooth, red, glossy membrane with tiny punctate bleeding (Auspitz sign)

Psoriasis

- Plaque psoriasis
- Guttate psoriasis
- Pustular psoriasis
- Inverse psoriasis
- Nail psoriasis
- Erythrodermic psoriasis

Guttate psoriasis

- Abrupt acute eruption of small (< 1 cm) psoriatic lesions
- Typically child or young adult with no history of psoriasis
  - Less commonly, guttate flare occur in preexisting psoriasis
- Primarily the trunk
- Strong association with recent strep infection with serologic evidence* (26-58 %)

Telfer NR; Chalmers RJ; Whale K; Colman G The role of streptococcal infection in the initiation of guttate psoriasis. Arch Dermatol 1992 Jan;128(1):39-42

Parapsoriasis

A Complex Issue

- **Resembles Psoriasis (red, scaly)**
- **Unrelated to pathogenesis, histopathology or treatment**

- **Large Plaque Parapsoriasis**
- **Small Plaque Parapsoriasis**
- **Pityriasis Lichenoides**
  - **Pityriasis lichenoides et varioliformis acuta**
  - **Pityriasis lichenoides chronica**
- **Lymphomatoid papulosis**

Parapsoriasis

- Disease processes caused by T-cell–predominant skin infiltrates
- Large plaque parapsoriasis
  - ~ 10% progress to CTCL
  - indolent & progresses over years, sometimes decades
  - treatment recommended because it may prevent progression to CTCL
- Small plaque parapsoriasis
  - benign; rarely if ever progresses
  - lasts several months to years
  - can spontaneously resolve

Lichenoid skin eruptions

- Subcategory of papulosquamous skin disease
- Scale often subtle; papules tend to remain small & discrete
- Occasionally, confluent plaques may form

Lichen Planus

A disease characterized by "P-words":

- Plentiful
- Pruritic
- Polished
- Purple
- Polygonal
- Planar
- Papules

Lichen planus

- Flexor surfaces of upper extremities
- Wickham stria: fine, white lines on papules
- Pruritus common but varies in severity
- > 50% resolve within 6 months
- 85% subside within 18 months
- Other areas of involvement:
  - Mouth: white or gray streaks forming linear or reticular pattern
    - may be asymptomatic, burning or painful
  - Genital
  - Nail plate thinning, grooving, ridging, pterygium
  - Cicatricial alopecia

Eczematous Drug Eruption

- Gold: lichenoid features
  - may progress to erythroderma
- Bleomycin
- Penicillin, chloramphenicol
- Quinine
- β-blocker
- Methyldopa
- Clonidine

SYSTEMIC ALLERGIC CONTACT DERMATITIS

Localized or generalized inflammatory skin disease

in contact sensitized individuals when exposed to the hapten orally, transcutaneously, intravenously or by inhalation

Dermatitis with Scattered Generalized Distribution

- Difficult diagnostic and therapeutic challenge: lacks the characteristic distribution that gives a clue to the etiology
- NACDG data: ~ 15% of the patients patch tested only had scattered generalized dermatitis
  - 49% had a positive patch test deemed at least possibly relevant to their dermatitis
  - The prevalence was higher in patients with a history of atopic dermatitis
  - Two most common allergens:
    - Nickel
    - Balsam of Peru

Zug KA, Rietschel RL, Warshaw EM, et al. The value of patch testing patients with a scattered generalized distribution of dermatitis: Retrospective cross-sectional analyses of North American Contact Dermatitis Group data, 2001 to 2004. J Am Acad Dermatol 2008;59:426-431

Allergens Associated with Food

NACD Allergen	Reactions
Nickel sulfate 2.5%	38 (48.7%)
Myroxilon pereirae 25%	20 (25.6%)
Propylene glycol 30%	5 (6.4%)
Fragrance mix 12%	4 (5.1%)
Compositae mix 6%	3 (3.9%)
Cinnamic aldehyde 1%	2 (2.6%)
Potassium dichromate 0.25%	2 (2.6%)
Sesquiterpene lactone mix 0.1%	2 (2.6%)

Warshaw E M et al. Contact Dermatitis Associated with Food: Retrospective Cross-Sectional Analysis of North American Contact Dermatitis Group Data, 2001–2004
Bauer A, Geier J, Elsner P. Type IV allergy in the processing industry: sensitization profiles in bakers, cooks and butchers. Contact Dermatitis 2002;46:228–35.

Food-related allergen: Nickel (most common)

- Top 3 body sites in patients with (+) PT
  - generalized (systemic contact dermatitis)
  - hands (vesicular hand dermatitis)
  - arms (direct physical contact with foods)
- Metal utensils leach nickel esp with acidic foods

Warshaw E M et al. Contact Dermatitis Associated with Food: Retrospective Cross-Sectional Analysis of North American Contact Dermatitis Group Data, 2001–2004

Bauer A, Geier J, Elsner P. Type IV allergy in the processing industry: sensitization profiles in bakers, cooks and butchers. Contact Dermatitis 2002;46:228–35.

*Jensen CS, Menne´ T, Johansen JD. Systemic contact dermatitis after oral exposure to nickel: a review with a modified meta-analysis. Contact Dermatitis 2006;54:79–86.

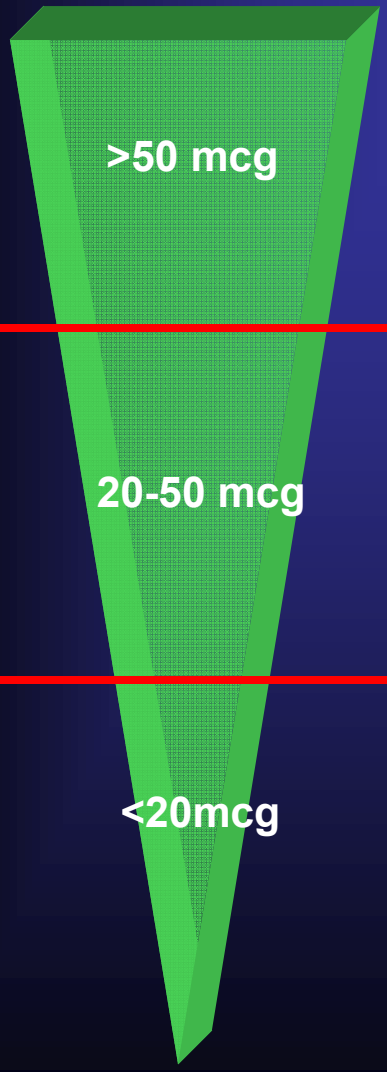
Di Giacchino M, Masci S, Cavalucci E, et al. Immuno-histopathologicchanges in the gastrointestinal mucosa in patients with nickel contact allergy. G Ital Med Lav 1995;17:33–6.

Dietary Nickel: Most Common Food Related Allergen

- Evidence support the contribution of dietary nickel to vesicular hand eczema
- Meta-analysis of systemic contact dermatitis following oral exposure to nickel estimated reaction in:
  - 1% of nickel allergic patients in a normal diet (0.3 - 0.6 mg/d)
  - 10% to 0.55 - 0.89 mg of nickel *
  - ~ 50% would flare after 2.5 mg nickel
- Case control study of 60 patients found endoscopic bowel inflammation in the oral-sensitive nickel-allergic patients

Kornik R & Zug K. Dermatitis2008;19(1):3-8
* Jensen CS, Menné T, Johansen JD. Systemic contact dermatitis after oral exposure to nickel: a review with a modified meta-analysis Contact Dermatitis 2006;54:79–86

Nickel Pyramid



>50 mcg

Soybean, Boiled ~ 1 cup: 895mcg
Cocoa, 1 tbsp: 147 mcg
Cashew, ~ 18 nuts:143 mcg

Figs ~5: 85 mcg
Lentils ½ cup cooked: 61 mcg
Raspberry: 56 mcg

20-50 mcg

Vegetables, canned½ cup: 40 mcg
Lobster 3 oz: 30 mcg
Peas Frozen, ½ cup: 27 mcg

Asparagus, 6 spears: 25 mcg
Oat Flakes 2/3 cup: 25 mcg
Pistachios, 47 nuts: 23 mcg

<20mcg

Strawberries, 7 med: 9 mcg
Bread wheat, 1 slice: 5 mcg
Poultry, 3.5 oz: 5 mcg
Carrots, 8 sticks: 5 mcg
Apple, 1 med: 5 mcg

Cheese 1.5 oz:3 mcg
Yogurt, 1 cup:3 mcg
Mineral water, 8 fl oz: 3 mcg
Mushroom raw, ½ cup: 2 mcg
Corn Flakes, 1 cup: 2mcg

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Fragrance: Food-related Allergen

- Myroxilon pereirae (Balsam of Peru)
  - One of 5 most prevalent allergens in TT
  - Found in toothpaste, mouthwash, flavors
  - Sensitization to BOP in cosmetics may lead to future systemic ACD flares from foods containing BOP
- Cinnamic aldehyde
  - Relatively specific (but not very sensitive) marker for spice allergy
  - Flavoring in gums, mouthwashes, toothpastes
- Fragrance mix

All 3 account for 33.3% of food related reactions

Warshaw E M et al. Contact Dermatitis Associated with Food: Retrospective Cross-Sectional Analysis of North American Contact Dermatitis Group Data, 2001–2004
Bauer A, Geier J, Elsner P. Type IV allergy in the processing industry: sensitization profiles in bakers, cooks and butchers. Contact Dermatitis 2002;46:228–35.

Fragrance Systemic Contact Dermatitis

~ 50% of patients with (+) PT to Myroxilon who followed BOP reduction diet had significant improvement of their dermatitis

Foods to Avoid in Balsam-Restricted Diet

- **Citrus fruits: oranges, lemons, grapefruit, tangerines, marmalade, juices**
- **Flavoring agents: pastries, bakery goods, candy, chewing gum**
- **Spices: cinnamon, cloves, vanilla, curry, allspice, anise, ginger**
- **Spicy condiments: ketchup, chili & barbecue sauce, chutney, pickles, pizza**
- **Perfumed or flavored tea & tobacco**
- **Chocolate**
- **Certain cough medicines & lozenges**
- **Ice cream**
- **Cola, spiced soft drinks such as Dr Pepper**
- **Tomatoes & tomato-containing products**

Salam TN, Fowler JF Jr. Balsam-related systemic contact dermatitis J Am Acad Dermatol. 2001 Sep;45(3):377-81

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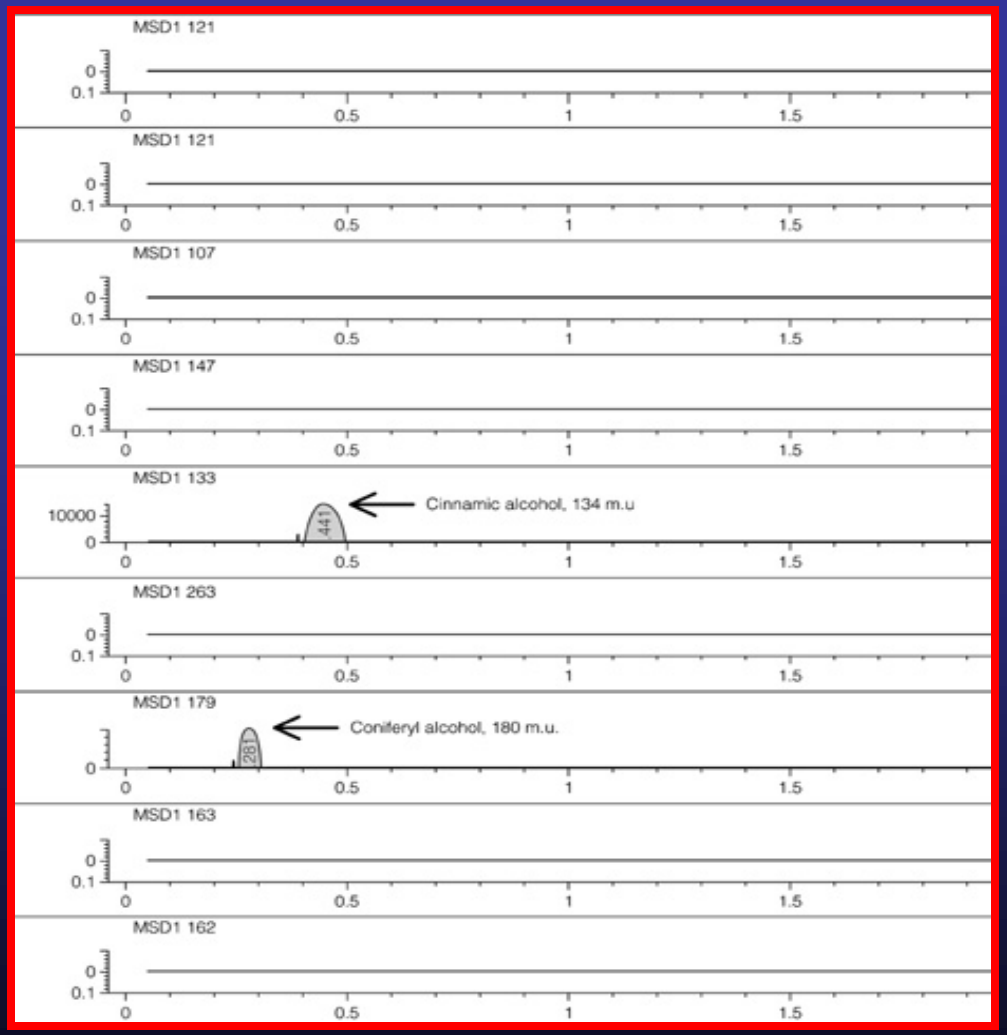
Mass spectrometry: Tomato peaks at 134 & 180 molecular weight corresponded to cinnamic alcohol & coniferyl alcohol



Srivastava D, Cohen D. Identification of the Constituents of Balsam of Peru in Tomatoes. Dermatitis April 2009. 20;02: 99-105

Medications, Doses and Patch-Test Results

Pt	Medication	Dose*	Reaction	Allergens	Improved
1	Prednisone	10	+++	Balsam of Peru	Yes
2	Pred + cyclosporine	10 / 200	+++	Cobalt chloride neomycin, Nickel	Yes
3	Cyclosporine	200†	+++	Cobalt chloride Carba mix; thiuram mix; tetraethylthiuram	Yes
4	Infliximab	5‡	+++	n,ndisulfide ′-diphenyl-4-phenylenediamine; zinc diethyldithiocarbamate	Yes
5	Prednisone	10	++	p-Phenylenediamine, Disperse Orange 3	Yes
6	Prednisone	10	++	Formaldehyde, Grotan BK, benzalkonium chloride	Yes
7	Cyclosporine	300§	++	Cinnamyl alcohol	Yes
8	Prednisone	10	+	Benzophenone-4, Grotan BK, cocamide DEA, CAPB, oleamidopropyl dimethylamine, Reactive Black 5, dimethylol dihydroxyethyleneurea (aq & FIX NF, modified Fix ECO), melamine formaldehyde	No
9	Prednisone	5	+	Euxyl K400, balsam of Peru, nickel oleamidopropyl dimethylamine, carba mix, potassium DC,	No
10	Mycophenolate Off Mycophenolate	2000 -	+ ++ +	Cobalt, gold, triethanolamine Formaldehyde MCI/MI; diazolidinylurea, DMDM hydantoin, melamine formaldehyde	No Yes
11	Prednisone	10	?	Fragrance mix, methyl methacrylate	Yes

? = questionable; aq = aqueous; DEA = diethanolamine; DMDM = dimethylol dimethyl; MCI/MI = methylchloroisothiazolinone/methylisothiazolinone; *All meds (mg/d) continued during PT unless otherwise indicated. †D/cd 2 days prior to testing.‡5 mg/kg/d. Patient on infusion q 8 wks; last dose 3 weeks prior to PT. §D/cd the day of PT

Rosmarin D, GottliebA et al . Patch-Testing While on Systemic Immunosuppressants. Dermatitis 20: 05, 265-270 .Oct 2009

Diagnosis of Contact Dermatitis: Patch Testing to Cosmetics

Agent	Test Concentration
Leave on cosmetics (make up, perfume, moisturizer, deodorants)	As is
Wash off cosmetics (soap, shampoo, bubble baths)	1%
Products with volatile solvents (hairspray, mascara, nail polish)	Dry then as is
Clothing, shoes, gloves	As is, moisten in saline
Plants & foods	As is; garlic & onion at 50% dilution

Use of supplementary allergens/ personal products:

- 16.3% of cosmetic-allergic patients only reacted to a non-NACDG allergen
- ~ 1/3 of allergic contact cheilitis had relevant (+) PT to non- NACDG series, including personal products (especially lip products), food & oral hygiene

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Recommendation Prior to Patch Testing
"Lo.C.A.L. (Low contact allergen) Skin Diet (Zug KA)

Eliminates most common allergens:

- **Fragrance**
- **Formaldehyde Releasing Preservatives**
- **MCI/MI**
- **MDG/PE**
- **Lanolin**
- **CAPB**
- **Benzophenone-3**

- Cover girl clean fragrance free liquid make-up
- Clinique blushing blush powder blush
- Clinique soft pressed eye shadow
- Max factor vivid impact lip liner-all shades
- Almay hypoallergenic roll-on anti-perspirant/ deodorant
- Cerave moisturizing lotion/ vanicream
- Cetaphil gentle skin cleanser
- Free & Clear shampoo
- Free & Clear hair spray - firm hold

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TREATMENT OF CONTACT DERMATITIS

- Identify and avoid contact with allergens and irritants
  - Give exposure list (synonyms & sources)
- Alternatives & substitutions if possible
  - Cover nickel plated objects
  - Wash formaldehyde containing garments
  - Gloves & barriers

TREATMENT OF CONTACT DERMATITIS

- Acute Contact Dermatitis (wet, oozing lesions)
  - Aluminum sulfate & calcium acetate (Domeboro) in clean absorbent cloth 20-30 min as compress 2-3 x a day
  - or Oatmeal baths (Aveeno) in extensive areas
  - Oral corticosteroid if severe
  - Fluourinated steroids for 1-2 weeks

- Chronic contact dermatitis
  - Emolients to decrease itching
  - Low to medium strength topical cs
  - Antihistamines to decrease itching
  - UV light
  - Cyclosporine
  - Topical calcineurin inhibitors

ACDS
Contact Allergen Management Program (CAMP)

Topical Skin Care Product Database

American Contact Dermatitis Society
info@contactderm.org

Allergists who need reference from ACDS member, send CV:
Luz Fonacier, MD. Head of Allergy Winthrop University Hospital
Professor of Clin Medicine, SUNY at Stony Brook
lfonacier@winthrop.org

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